

# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see form PCT/ISA/220

12-10-05

PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY  
(PCT Rule 43bis.1)

Date of mailing

(day/month/year) see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference  
see form PCT/ISA/220

## FOR FURTHER ACTION

See paragraph 2 below

International application No  
PCT/US2005/004270

International filing date (day/month/year)  
09 02 2005

Priority date (day/month/year)  
10 02 2004

International Patent Classification (IPC) or both national classification and IPC  
C12N15/11, C12P19/34, C07H21/02, C07H21/04, A01N43/04, A61K31/713

Applicant  
SIRNA THERAPEUTICS, INC.

### 1. This opinion contains indications relating to the following items:

- ☒ Box No I Basis of the opinion
- ☐ Box No II Priority
- ☐ Box No III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No IV Lack of unity of invention
- ☒ Box No V Reasoned statement under Rule 43bis 1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No VI Certain documents cited
- ☐ Box No VII Certain defects in the international application
- ☐ Box No VIII Certain observations on the international application

### 2. FURTHER ACTION

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66 1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220

### 3. For further details, see notes to Form PCT/ISA/220

Name and mailing address of the ISA:



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**Box No. I Basis of the opinion**

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1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material:
    - ☒ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material:
    - ☐ in written format
    - ☒ in computer readable form
  - c. time of filing/furnishing:
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☒ furnished subsequently to this Authority for the purposes of search.
3. ☒ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No  
PCT/US2005/004270

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**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

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**1. Statement**

Novelty (N)	Yes: Claims	1-32
	No: Claims	
Inventive step (IS)	Yes: Claims	1-32
	No: Claims	
Industrial applicability (IA)	Yes: Claims	1-32
	No: Claims	

**2. Citations and explanations**

**see separate sheet**

**Re Item V**

**Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

The documents mentioned in the present Written Opinion / International Preliminary Examination Report are numbered as in the International Search Report. D1 corresponds to the first document of the Search Report, D2 to the second document etc.

1. The document D1 or D2 can be regarded as being the closest prior art to the subject-matter of claim 1 and 2. Both documents show bispecific siRNA constructs containing two monospecific siRNA sequences containing loops separated by an intervening single stranded spacer sequence.
2. The multifunctional siNA molecules of formulas I and II as described in claims 1 and 2 differ from D1 and D2 in that said multifunctional siNA consist of two annealed, single stranded sequences wherein each sequence has its own 3' and 5' end which are not connected by loop structure.
3. The subject-matter of claims 1 and 2 is therefore new (Article 33(2) PCT).
4. The problem to be solved by the present invention may be regarded as the provision of further multifunctional siNA molecules.
5. The solution to this problem proposed in claims 1 and 2 of the present application is considered as involving an inventive step (Article 33(3) PCT) since the prior art does not contain any indication that would prompt the skilled person to provide siNA molecules of formula I and II. Claims 1 and 2 are therefore inventive.
6. Claims 3-32 are dependent on claims 1 and 2 and as such also meet the requirements of the PCT with respect to novelty and inventive step.

**The attention of the applicant is drawn to the fact that a reply to this opinion is only expected if he intends to file a chapter II demand.**